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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
ANGELL, JON E	

ART UNIT	PAPER NUMBER
1635	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/672,144	TAMARKIN ET AL.	
	Examiner	Art Unit	
	J. E. Angell	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This Action is in response to the communication filed on 12/29/2008.

Claims 27-35 are currently pending ad are addressed herein.

Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

Election/Restrictions

Applicant's election without traverse of the combination of biologically active factors that is TNF-alpha and IL-12 in the reply filed on 1/3/2007 is acknowledged.

Claims 27-35 as they are drawn to the elected combination of factors are examined herein.

Drawings

The petition for color drawings and color drawings was received on 4/17/2008. The petition for color drawings has been GRANTED.

/JD Schultz/

Supervisory Patent Examiner, Art Unit 1635

Priority

1. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e), 120, 121, or 365(c) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 08/215,030, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The instant claims are drawn to a method for delivery of more than one biologically active factor comprising administering to a human or animal a composition comprising more than one biologically-active factor and a target molecule admixed with or bound to a colloidal metal wherein the more than one biologically active factor is TNF-alpha and IL-12 and wherein the colloidal metal is colloidal gold. 08/215,030 was searched but support for the instant claimed invention was not found. Should Applicants traverse, they should

to provide the page and line numbers where support for the instant claims can be found in the priority document(s).

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 27-35 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 94/21288 (cited by Applicants) as evidenced by Van Den Pol (Quarterly Journal of Experimental Physiol. 1984, 69:1-33) and NCBI MeSH, Tumor Necrosis Factor-alpha (see www.ncbi.nlm.nih.gov/sites/entrez?db=mesh&cmd=search&term=tumor%20necrosis%20factor) and WO 95/249118.

As indicated above, the instant claims do not receive the benefit of priority to Application No. 08/215,030. Therefore, the instant rejection under 35 U.S.C. 102(b) is appropriate.

The instant claims are drawn to a method for the delivery of more than one biologically-active factor (including treating cancer or an immune disease) comprising administering to a human or animal a composition comprising more than one biologically-active factor and a target molecule admixed with or bound to a colloidal metal wherein the more than one biologically active factor is TNF-alpha and IL-12 and wherein the colloidal metal is colloidal gold. It is

noted that at least on of the biologically active factors can be the targeting molecule (see claim 29).

WO 94/21288 teaches a composition and method that allows the administration of a biologically active factor to a human or animal without the normal toxic side effects by admixing the biologically active factor and a colloidal metal such as colloidal gold. WO 94/21288 teaches that the present invention can be used to treat a disease with a biologically active factor or a **combination of biologically active factors** (emphasis added), see Abstract. WO 94/21288 teaches that the present invention can be used to treat cancer or immune disease (e.g., see claim 19).

WO 94/21288 teaches that current therapies which comprise administering biologically-active factors to a human or animal are somewhat effective yet produce significant toxic side effects. Further, the toxic side effects limit the amount of antigen that may be administered, and therefore limit the efficacy of the therapy. Additionally, the toxicity of some biologically active factors precludes their use in such therapies. WO 94/21288 teaches that the combination of a colloidal metal with such biologically-active factors reduces toxicity while maintaining or increasing the therapeutic results thereby improving the efficacy as higher concentrations of biologically-active factors may be administered, or by allowing the use of **combinations of biologically-active factors** (emphasis added). WO 94/21288 teaches that the use of colloidal metals in combination with biologically-active factors therefore allows the use of higher concentrations of biologically-active factors or formerly unusable toxic substances, to be administered to humans or animals, see p.6, lines 23-31.

WO 94/21288 specifically teaches that IL-12 and Tumor Necrosis Factor as well as other biologically active factors can be used (e.g., see p.5, lines 17-28 and claim 4).

WO 94/21288 teaches that biologically active factor IL-1 mixed with colloidal gold retains its biological activity when administered *in vitro* to MCF-7 cells, see Example VI and Figure 2.

WO 94/21288 teaches that biologically active factor IL-6 efficiently binds colloidal gold, see Example VII.

Van Den Pol teaches that colloidal gold particles maintain a negative charge, and adsorb irreversibly to large protein molecules in solution. Gold particles will also adsorb to small proteins, but may not be stable and the gold may flocculate with time. Gold adsorbed to small proteins can be stabilized by the addition of a non-specific protein like bovine serum albumin, see p. 4, 4th para.

NCBI MeSH teaches that Tumor Necrosis Factor is another name for Tumor Necrosis Factor-alpha.

WO 95/249118 9/21/95 teaches that IL-12 known in vivo activities of IL-12 include increased survival in SCID mice, cure of leishmaniasis in susceptible strains of mice and suppresion of tumor growth. Thus, IL-12 is a chemotherapeutic agent.

Given that WO 94/21288 teaches IL-12 and TNF-alpha and combinations of these factors with colloidal gold and given Van Den Pol teaches that the negative charge of gold particles allows for protein binding, the product of the prior art comprises the same product as claimed in the instant invention, that is, a composition comprising IL-12 and TNF-alpha bound to a colloidal metal platform, thus the claimed product is anticipated because the product will

inherently be a targeted delivery composition comprising one or more effector molecules and one or more cell-specific targeting molecules bound to a colloidal metal platform; wherein the one or more effector molecules and the one or more cell specific targeting molecules are distinct molecules. See Ex parte Novitski 26 USPQ 1389 (BPAI 1993). Although the reference does not specifically state that the biologically active factors IL-12 and TNF-alpha bound the colloidal gold, the product used in the claimed method appears to be the same as the prior art product, absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed method. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product and methods of its use are different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA).

Given that WO 94/21288 teaches using combinations of the biologically active factors of the instant invention, which include IL-12 and TNF-alpha, methods of delivery using the colloidal gold composition *in vitro* and *in vivo* to a cell specific or target site, and methods for reducing systemic toxicity of toxic biological active factors WO 94/21288 anticipates the instant claims.

Response to Arguments

1. Applicant's arguments filed 4/17/2008 have been fully considered.

2. Regarding the Double Patenting rejection, it is noted that Application 09/189,657 is now abandoned. Therefore, the Double Patenting rejection is withdrawn.

3. Regarding the rejection of claims under 35 USC 102(b), Applicants argue that the rejection is improper because the instant application claims priority to U.S. Application No. 08/215,030. However, as indicated herein, the instant claims do not receive the benefit of priority to U.S. Application No. 08/215,030. Therefore, the rejection is appropriate.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is 571-272-0756. The examiner can normally be reached on Monday-Thursday 8:00 a.m.-6:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/J. E. Angell/

Primary Examiner, Art Unit 1635